United States Department of the Interior

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Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Drive, Room 1-23
Rockville, MD 20857

SUBJECT: Comments on the Draft Document "Proposals to Increase the Availability of Approved Animal Drugs for Minor Species and Minor Use" (Docket No. 97N-0217)

The Center for Veterinary Medicine (CVM) is to be commended for their efforts to propose additional and potentially less restrictive methods to gain approvals for a variety of minor use drugs. I enthusiastically endorse these attempts and offer my comments to your Discussion Draft document "Proposals to increase the availability of approved drugs for minor species and minor uses (Docket Number 97N-0217).

A. Modification of Extralabel Provisions

Question *Will the proposed modification of extralable provision and suggested sunset period provide adequate and appropriate temporary relief until approved products are made available, or will it serve as a disincentive to the pursuit of approvals?*

Comment: Extralabel use of medicinal drugs in aquaculture is appropriate both on humanitarian and ethical grounds. Their use under a sunset clause is appropriate, however it seems that some additional incentives should be included to ensure continued progress to an extended or expanded approval. The length of the sunset period could be uniformly applied or it could be set on a case-by-case basis at the discretion of the Agency. In any event, the period of time for each chemical should begin at the start of a commitment from the sponsor to expand or extend the label. There should be provisions for regulatory discretion to evaluate the process to ensure that there is reasonable progress in the approval process during the sunset period.

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B. Removal of Disincentives

Question *Will the suggested strategies be sufficient to remove the existing direct regulatory disincentives? Are there additional disincentives to gaining approvals that should be removed? How might this be accomplished?*

Comments: The Center for Veterinary Medicine advocates that disincentives be removed by 1) increasing enforcement, 2) remove unapproved drugs from the market, and 3) remove or reduce the risk of a minor species approval jeopardizing an older and original major species approval. Because there are so few drugs now approved for aquaculture, increased enforcement may not be an appropriate use of Agency resources. Enhancing efforts under proposal 3 above may be more productive in allowing the broader use of drugs already approved for use.

C. Enhancement of Existing Programs for Data Development

Questions: *Are there additional existing congressional research funds which could be expanded for minor use research? Would the proposed model program provide a useful supplement to the existing NRSP-7 program? Would the established data bases be useful to parties interested in furthering approval of minor use products? If so, how might it be developed most cost-effectively?*

Comments: Appropriations for the budgets of NRSP-7, Saltonstall-Kennedy Grant Program, and National Coastal Research Institute should be expanded but with funds marked for use to develop minor use drugs. Additional funding should be considered to support the budgets of two federal laboratories that have substantial existing programs and expertise in the development of aquaculture drug approvals -(Public Aquaculture - Upper Mississippi Science Center-La Crosse, Biological Resources Division, U.S. Geological Survey, U.S. Department of the Interior; Private Aquaculture - Stuttgart National Aquaculture Research Center, Agricultural Research Service, U.S. Department of Agriculture). The NRSP-7 project leaders should ensure that focused, concerted, and sustained efforts be made to ensure that timely drug approvals are generated from efforts made by that group.

A minor drug use data base would be useful, but should not be established at the expense of other proposals that would support minor use drug research and development.

D. Incentives to Pursue Minor Use Drug Approvals

Questions: *Is the benefit of extended exclusivity, with respect to fostering initial approval, more important than the risk of increased drug cost that could be associated with decreased competition from generic approvals? Would it be a more significant incentive to provide for an extended*

period of exclusivity for all the claims of the product.

Comments: Incentives to pharmaceutical firms or other drug sponsors, either small or large, are and will continue to be extremely important to the development of minor use drugs. Incentives should always be considered to ensure that effective drugs, properly used can be as widely available as possible. One major problem with the development of drugs for minor uses is the lack of sufficient return on investment. By allowing for a variety of fiscal incentives, drug sponsors should be more willing to bring a greater number of drugs into the minor use arena.

E. Data Sharing by Major Species NADA Holders

Questions: *Is it fair to require the sharing of data? How could potential liability be ameliorated under such a data sharing system?*

Comments: The Food, Drug, and Cosmetic Act should be amended to allow CVM to consider appropriate data from major drug applications when reviewing NADAs for minor uses once the drug is in the generic classification, or when the approval has been abandoned or withdrawn. The lack of access to expensive existing data is a major impediment to gaining minor species approvals. Once a drug has reached generic status there should be some mechanism for potential sponsors of minor species drugs to access data developed for a prior submission as long as the data adequately address current guideline standards. By denying access to existing acceptable data, inefficiencies are created into the market that deny the most efficient <u>total</u> use of a drug.

F. Creation of a Statute of a "Minor Use Animal Drug" Program

Questions: *Would a statutory designation of a "minor use animal drug" similar to the designation of "human orphan drug" be useful? Are the incentives associated with this strategy a necessary component of the overall proposed "Minor Use Animal Drug Program"?*

Comments: The statutory designation of a *"minor use animal drug"* should be highly embraced and endorsed. Part of the problem with development of minor use drugs is the perception that there is no or little interest in the development of these types of drugs on the part of industry or on the part of the Agency. With a position within the Office of New Animal Drug Evaluation that would act as a contact and clearinghouse for information within the Agency for minor use drug sponsors, there will be less reluctance on the part of potential sponsors to seek to develop new minor use drugs.

G. Conditional Approval for Minor Uses Involving Non-Food Animals

Questions: *Would the proposed constraints upon conditional approval provide sufficient consumer protection and still provide adequate incentive to pursue a conditional drug approval to final approval? Is the proposed*

process appropriately restricted to minor uses involving non-food animals?

Comments: Conditional drug approvals for non-food animals should be allowed and additional mechanisms to accomplish this should be encouraged. Moreover, the Agency should consider allowing treatment of certain life stages of food fish (i.e. gametes, eggs, larvae, fry, and fingerlings) to this category. Whether to allow a drug to be developed for use under non-food alternative approval processes or under a category of non-food life stages should be considered by the Agency on a case-by-case basis by drug. Many of the bulk drugs proposed for external use in aquaculture are not likely to pose significant residue chemistry problems because of their physico-chemical properties.

Alternative methods to address non-human health related guidelines should be considered to allow complete approval in minor use species. Requirement to address guidelines in the areas of target animal safety and efficacy could be addressed in a less formal manner without reducing the requirements to address guidelines for human health.

H. Alternate Approval Standard/Expert Review Panels for Minor Uses Involving Non-Food Animals.

Questions: *Will animal caretakers find drugs approved under the proposed alternate standard (with associated restrictions) be acceptable? Dot the affected industries have the needed expertise and/or will they be willing to fund the expert review panels? Is the proposed process appropriately restricted to minor uses involving non-food animals?*

Comments: All individuals involved with aquaculture would find an approved drug more acceptable than using a drug under Extralabel Use or under Low Regulatory Priority uses as long as the standards under which the drugs were approved were accepted by both a panel of knowledgeable experts and reviewed and accepted by CVM staff scientists. Leading aquaculture professionals, in both the public and private sectors, who have been involved in the industry for a sustained period, possess the professional expertise to review target animal safety and efficacy data. An expert review panel composed of scientists from professional fishery or veterinary societies would be most appropriate. The Agency should consider review of both target animal safety and efficacy studies for drugs intended for use on food animals by a similar Expert Review Panel since neither of the guidelines would have a direct impact on human health. Reviews of product chemistry, mammalian toxicology, environmental fate and effects, and human health guidelines would be conducted in a traditional review format.

I. International Harmonization

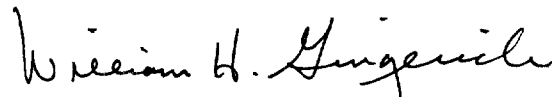
Questions: *Could non-government input facilitate equivalency determinations? Are there sufficient numbers of foreign approvals to justify establishing this*

program?

Comments: I support any initiative by CVM to address harmonization issues among the world trading community, particularly among strong trading partners. As the world community becomes one, it is more imperative than ever that a common world food supply have common or equivalent guidelines. The issue of equivalency and commonality among the international community will not go away, it will only continue to grow. CVM should consider taking every opportunity to join international dialogs on harmonization of their guidelines with those of other countries. This is especially true with countries that are strong trading neighbors.

I wish to commend the efforts of CVM and particularly the ADAA Minor Use/Minor Species Working Group. The task they have undertaken is not easy, but the benefit to minor species and minor use issues can be great. Their hard work on this draft discussion document is appreciated by those of us who will benefit from the proposed changes away from outdated or unnecessarily restrictive food and drug laws. I encourage FDA and CVM to consider these changes seriously and to actively continue to seek ways in which the food and drug laws may be changed to more readily accommodate minor species and minor drug issues.

Sincerely yours,



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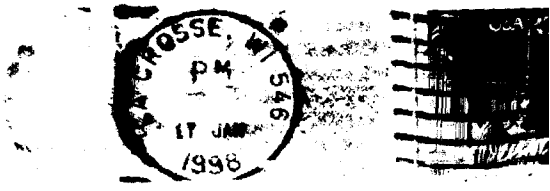

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